ABSTRACT OF THE DISCLOSURE

Recombination in mammalian somatic cell chromosomes is promoted and marked by a method called mosaic analysis with double marker (MADM). Mouse "knock-in" techniques are used to create pairs of chromosomes in which recombinase target sites are placed at homologous chromosomal locations. The knock-in constructs are engineered so that cellular markers, such as green or red fluorescent protein (GFP or RFP), are only expressed after recombinase -induced recombination. This system provides high-sensitivity detection of recombinase-induced mitotic recombination, even down to the single cell level. When this recombination is induced in a mouse heterozygous for a mutation in a gene distal to the "knock-in" locus on the same chromosome, it results in homozygosity of this mutation in the labeled cells. This allows the analysis in singly-labeled neurons of genes whose pleiotropic effects might otherwise result in early lethality.